U.S. FOOD & DRUG ADMINISTRATION

# Memorandum

**TO:** OMB reviewers

**FROM:** FDA

**DATE:** July 27, 2017

**SUBJECT:** Background on FDA Guidance for Industry #236, "**Regulation of Mosquito-Related Products**"

## BRIEF SUMMARY

FDA, in consultation with EPA, has prepared a final guidance for industry to clarify that the regulatory oversight of products intended to prevent, destroy, or repel mosquitoes for population control purposes resides with EPA.

## BACKGROUND

Currently, FDA has jurisdiction over certain mosquitoes that have been altered to have pesticidal properties. For example, FDA has been regulating a species of mosquitoes that has been genetically engineered (GE) so that release of male GE mosquitoes cause a suppression of the mosquito population in the release area over time. In response to stakeholder comment, FDA has worked with EPA to issue draft guidance clarifying the regulatory oversight of mosquito-related products. The comment period for the draft guidance closed on February 21, 2017. FDA and EPA would like to finalize this guidance to remove regulatory uncertainty for developers and help facilitate innovation in this space.

### A. History of Animal Drug/Pesticide Issue

Until the mid-1970s, products intended to kill "pest" animals met the definition of both a pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and a drug under the Federal Food, Drug, and Cosmetic Act (FD&C Act). That is because the FD&C Act defines the term "drug" as, among other things, "articles (other than food) intended to affect the structure or any function of the body of man or other animals." Any article whose intended use is to, for example, kill, harm, incapacitate, or sterilize insects, rodents, or other animals meets the definition of drug under the FD&C Act because it is intended to affect the structure or function of the body of the animal.

In the mid-1970s, to clarify jurisdiction and avoid duplicative regulation of products like those used to treat "pest" animals, Congress amended the FIFRA pesticide definition to exclude new animal drugs. This could be interpreted to mean that many traditional insecticides and other pesticides that have always been regulated by EPA are in fact excluded from the FIFRA definition of "pesticide" because they meet the "intended to affect the structure or any function of the body of … animals" prong of the

drug definition. Since enactment of this amendment, FDA and EPA have regulated products under a framework that the agencies developed to avoid duplication prior to the change in the statute.

In January 2009, FDA issued a final guidance for industry on the regulation of genetically engineered (GE) animals, explaining the process by which FDA regulates GE animals and providing recommendations to producers of GE animals. FDA regulates GE animals under the new animal drug provisions of the FD&C Act. Because the genetic material, or recombinant DNA (rDNA) construct, used to engineer the animal is intended to affect the structure or function of that animal, the rDNA construct meets the definition of a drug in the FD&C Act.

## B. U.S. Coordinated Framework for Regulation of Biotechnology and the Regulation of GE Animals

In 1986, with the advent of genetic engineering and to support then-emerging technology, the White House Office of Science and Technology Policy (OSTP) issued the *Coordinated Framework for Regulation of Biotechnology*, which outlined a comprehensive Federal regulatory policy for ensuring the safety of biotechnology products. Updated in 1992, the Coordinated Framework explains the proper allocation and coordination of oversight responsibilities under the relevant statutes and among the relevant Federal agencies. The goal of the 1992 *Coordinated Framework* has been to ensure public confidence in the regulatory system and to prevent unnecessary barriers to future innovation and competitiveness by improving the transparency, coordination, predictability, and efficiency of the regulation of biotechnology products while continuing to protect health and the environment.

Advances in science and technology have dramatically altered the biotechnology landscape in the last decade, greatly enhancing the ease, speed and precision with which new products can be developed. Therefore, in 2015, the OSTP started a process to re-examine and update the Coordinated Framework and develop a national strategy to prepare for future products of biotechnology. The *Update to the Coordinated Framework for Regulation of Biotechnology* and the *National Strategy for Modernizing the Regulatory System for Biotechnology Products* were issued in 2016-2017 by FDA, EPA, and USDA—the primary agencies that regulate the products of biotechnology— and represent the United States government's efforts to modernize the federal regulatory system for biotechnology.

As part of this work, FDA, EPA, and USDA have committed to clarifying the regulation of GE insects under our current authorities. Since then, FDA and EPA have considered mechanisms that would enable EPA to regulate mosquito-related products, including GE mosquitoes, under FIFRA when the developer claims they are intended to prevent, destroy, repel, or mitigate mosquitoes for population control purposes, while FDA would continue to regulate mosquito-related products for other intended uses, including to prevent or mitigate disease transmission under the FD&C Act.

## C. Draft Guidance for Industry (GFI) #236

In January 2017, FDA released [ HYPERLINK "https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM533600.pdf" ], which clarifies that mosquito-related products intended to function as pesticides by preventing, destroying, repelling, or mitigating mosquitoes for population control purposes are not "drugs" under section 201(g)(1)(C) of the FD&C Act and, when the guidance is finalized, will be regulated exclusively by EPA as "pesticides" under FIFRA. FDA would continue to have jurisdiction over mosquito-related products intended to cure, mitigate, treat or prevent disease in man or other animals or to reduce the viral or pathogen load in a mosquito. FDA developed this guidance in coordination with EPA. This

interpretation is consistent with congressional intent, legally supportable, and provides a rational approach for dividing responsibilities between FDA and EPA in regulating mosquito-related products.

The comment period on the draft guidance ended on February 21, 2017. FDA received 18 comments, the majority of which are non-substantive or supportive of the agency's interpretation as discussed in the guidance. One comment from The Center for Food Safety (CFS) argues that FDA does not have jurisdiction over GE animals generally (including insects) under its new animal drug authority[1] but supports EPA regulation of GE mosquitoes.

## D. Oxitec GE Mosquito Product

Oxitec, Ltd. has an open Investigational New Animal Drug (INAD) file with CVM regarding a genetically engineered (GE) line of the mosquito *Aedes aegypti* (OX513A) with the intent of suppressing the population of that mosquito at the release site(s). This species of mosquito is known to transmit virus-caused diseases including Zika, dengue, yellow fever, and chikungunya.

In August 2016, FDA completed review of a draft environmental assessment (EA) that Oxitec submitted, and released a final EA and a Finding of No Significant Impact (FONSI) indicating that Oxitec's proposed investigational field release of these mosquitoes in Key Haven, Florida, would not have a significant impact on the environment. FDA worked in consultation with experts from other agencies, including CDC and EPA. Based on results of a public referendum in November 2016, the local mosquito control authority decided not to go forward with the proposed investigational release in Key Haven.

## E. Finalizing GFI #236

In light of the existing public health emergency declaration associated with the Zika virus outbreak, there is a sense of urgency and considerable interest in the use of novel vector control methods. Finalizing this guidance as soon as possible will provide regulatory clarity and help facilitate innovation in this space. The significance of finalizing GFI #236 includes:

- Eliminating uncertainty: Oxitec, other developers, and the general public would have greater clarity about which agency is responsible for regulation of particular mosquito-related products.
- Providing a clear and efficient regulatory pathway for the Oxitec GE mosquito product (and subsequent products that are intended to control mosquito populations): Finalizing GFI #236 allows for smooth transfer of the Oxitec product to EPA.

[1] This is consistent with the position CFS is taking in current litigation challenging FDA's approval of an application related to a GE Atlantic salmon.